



Clinical trial results:

An Open-label, Multi-center Study to Evaluate the Disease Free Survival Rate of a Perioperative Combination of Capecitabine (Xeloda), Trastuzumab (Herceptin) and Oxaliplatin (XELOX-Trastuzumab) in Patients With Resectable Gastric or Gastro-esophageal Junction Adenocarcinoma (stages II-IV).

Summary

| | |
|--------------------------|----------------|
| EudraCT number | 2009-017848-14 |
| Trial protocol | ES |
| Global end of trial date | 10 June 2014 |

Results information

| | |
|--------------------------------|---------------|
| Result version number | v1 (current) |
| This version publication date | 06 April 2016 |
| First version publication date | 06 April 2016 |

Trial information

Trial identification

| | |
|-----------------------|---------|
| Sponsor protocol code | ML25189 |
|-----------------------|---------|

Additional study identifiers

| | |
|------------------------------------|-------------|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT01130337 |
| WHO universal trial number (UTN) | - |

Notes:

Sponsors

| | |
|------------------------------|--|
| Sponsor organisation name | F. Hoffmann-La Roche AG |
| Sponsor organisation address | Grenzacherstrasse 124, CH-4070, Basel, Switzerland, |
| Public contact | Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 61 6878333, global.trial_information@roche.com |
| Scientific contact | Roche Trial Information Hotline, F. Hoffmann-La Roche AG, +41 61 6878333, global.trial_information@roche.com |

Notes:

Paediatric regulatory details

| | |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP) | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

Results analysis stage

| | |
|--|--------------|
| Analysis stage | Final |
| Date of interim/final analysis | 10 June 2014 |
| Is this the analysis of the primary completion data? | No |

| | |
|----------------------------------|--------------|
| Global end of trial reached? | Yes |
| Global end of trial date | 10 June 2014 |
| Was the trial ended prematurely? | No |

Notes:

General information about the trial

Main objective of the trial:

This was a Phase II, open-label, non-comparative, national, multicenter study with competitive recruitment to investigate the perioperative administration of one of the regimens considered to be standard in the treatment of Gastric Cancer (GC) in combination with trastuzumab.

Protection of trial subjects:

Participants willing to participate were informed of the nature of the trial in detail and thereafter signed the informed consent form.

Background therapy: -

Evidence for comparator: -

| | |
|---|------------------|
| Actual start date of recruitment | 16 July 2010 |
| Long term follow-up planned | Yes |
| Long term follow-up rationale | Safety, Efficacy |
| Long term follow-up duration | 25 Months |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

Population of trial subjects

Subjects enrolled per country

| | |
|--------------------------------------|-----------|
| Country: Number of subjects enrolled | Spain: 36 |
| Worldwide total number of subjects | 36 |
| EEA total number of subjects | 36 |

Notes:

Subjects enrolled per age group

| | |
|---|----|
| In utero | 0 |
| Preterm newborn - gestational age < 37 wk | 0 |
| Newborns (0-27 days) | 0 |
| Infants and toddlers (28 days-23 months) | 0 |
| Children (2-11 years) | 0 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 16 |
| From 65 to 84 years | 19 |

| | |
|-------------------|---|
| 85 years and over | 1 |
|-------------------|---|

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

Screening period comprised of 35 days. A total of 136 participants were included in the study out of which 36 participants were enrolled and 100 participants discontinued due to screening failures. Abbreviation of AE= adverse event.

Period 1

| | |
|------------------------------|--------------------------------|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Not applicable |
| Blinding used | Not blinded |

Arms

| | |
|-----------|--------------------------------------|
| Arm title | Capecitabine+Oxaliplatin+Trastuzumab |
|-----------|--------------------------------------|

Arm description:

Participants received 3 cycles of capecitabine (1,000 milligrams per meter squared [mg/m²] tablet orally [p.o] twice daily, Days 1-14)/oxaliplatin (130 mg/m² as a 120-minute intravenous [IV] infusion, Day 1 of the cycle)/trastuzumab (8 milligrams per kilograms [mg/kg] on Day 1, followed by doses of 6 mg/kg as IV infusion) (XELOX-trastuzumab) as neoadjuvant treatment, every 3 weeks, thereafter, they were assessed for surgery. After surgery, participants received 3 cycles of XELOX-trastuzumab as treatment adjuvant to the surgery, thereafter, another 12 cycles of trastuzumab as monotherapy, was administered every 3 weeks, until disease progression or death.

| | |
|--|--------------|
| Arm type | Experimental |
| Investigational medicinal product name | Capecitabine |
| Investigational medicinal product code | |
| Other name | Xeloda |
| Pharmaceutical forms | Tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Participants received capecitabine 1,000 mg/m² tablet p.o twice daily, Days 1-14, every 3 weeks.

| | |
|--|-----------------|
| Investigational medicinal product name | Oxaliplatin |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received oxaliplatin 130 mg/m² as a 120-minute IV infusion Day 1 of the cycle, every 3 weeks.

| | |
|--|-----------------|
| Investigational medicinal product name | Trastuzumab |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Infusion |
| Routes of administration | Intravenous use |

Dosage and administration details:

Participants received trastuzumab 8 mg/kg on Day 1, followed by doses of 6 mg/kg as IV infusion, every 3 weeks.

| Number of subjects in period 1 | Capecitabine+Oxalip latin+Trastuzumab |
|---------------------------------------|--|
| Started | 36 |
| Completed | 22 |
| Not completed | 14 |
| Consent withdrawn by subject | 3 |
| Disease progression | 1 |
| Death | 1 |
| Principal investigator decision | 1 |
| Toxicity, AE/intercurrent disease | 7 |
| Surgical resection (R2) | 1 |

Baseline characteristics

Reporting groups

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Capecitabine+Oxaliplatin+Trastuzumab |
|-----------------------|--------------------------------------|

Reporting group description:

Participants received 3 cycles of capecitabine (1,000 milligrams per meter squared [mg/m²] tablet orally [p.o] twice daily, Days 1-14)/oxaliplatin (130 mg/m² as a 120-minute intravenous [IV] infusion, Day 1 of the cycle)/trastuzumab (8 milligrams per kilograms [mg/kg] on Day 1, followed by doses of 6 mg/kg as IV infusion) (XELOX-trastuzumab) as neoadjuvant treatment, every 3 weeks, thereafter, they were assessed for surgery. After surgery, participants received 3 cycles of XELOX-trastuzumab as treatment adjuvant to the surgery, thereafter, another 12 cycles of trastuzumab as monotherapy, was administered every 3 weeks, until disease progression or death.

| Reporting group values | Capecitabine+Oxaliplatin+Trastuzumab | Total | |
|---|--------------------------------------|-------|--|
| Number of subjects | 36 | 36 | |
| Age categorical Units: Subjects | | | |
| Age Continuous Units: years arithmetic mean standard deviation | 63.44 ± 10.42 | - | |
| Gender, Male/Female Units: participants | | | |
| Female | 7 | 7 | |
| Male | 29 | 29 | |

End points

End points reporting groups

| | |
|---|--------------------------------------|
| Reporting group title | Capecitabine+Oxaliplatin+Trastuzumab |
| Reporting group description: | |
| Participants received 3 cycles of capecitabine (1,000 milligrams per meter squared [mg/m ²] tablet orally [p.o] twice daily, Days 1-14)/oxaliplatin (130 mg/m ² as a 120-minute intravenous [IV] infusion, Day 1 of the cycle)/trastuzumab (8 milligrams per kilograms [mg/kg] on Day 1, followed by doses of 6 mg/kg as IV infusion) (XELOX-trastuzumab) as neoadjuvant treatment, every 3 weeks, thereafter, they were assessed for surgery. After surgery, participants received 3 cycles of XELOX-trastuzumab as treatment adjuvant to the surgery, thereafter, another 12 cycles of trastuzumab as monotherapy, was administered every 3 weeks, until disease progression or death. | |

Primary: Percentage of Participants With Disease-free Survival (DFS) at Month 18

| | |
|-----------------|--|
| End point title | Percentage of Participants With Disease-free Survival (DFS) at Month 18 ^[1] |
|-----------------|--|

End point description:

DFS was the time elapsed from the time of surgery (for complete resection [R0] participants) until the date on which progression or death from any cause was documented (whichever occurred first). Progression was defined as target lesions greater than (>) 20 percent (%) increase in the sum of the longest diameter (SLD) taking as reference the smallest SLD recorded since the treatment started (nadir) and minimum 5 millimeter (mm) increase over the nadir. When the sum becomes very small, increases within the measurement error (2-3 mm) can lead to a 20% increase. Participants who did not present progression and who had not died were censored on the last date on which it was known that there was no progression (last response assessment). Intent-to-treat (ITT) population included all enrolled participants.

| | |
|----------------|---------|
| End point type | Primary |
|----------------|---------|

End point timeframe:

Month 18

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: As the study was non-comparative in nature, no statistical analysis was performed.

| | | | | |
|-----------------------------------|--------------------------------------|--|--|--|
| End point values | Capecitabine+Oxaliplatin+Trastuzumab | | | |
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 36 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 76.12 (57.72 to 87.32) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Complete Tumor Resection (R0)

| | |
|-----------------|---|
| End point title | Percentage of Participants With Complete Tumor Resection (R0) |
|-----------------|---|

End point description:

R0 resection was defined as having performed a complete resection of the tumor with adequate tumor-free margins and regional lymph node extirpation. ITT population. Here "number of participants analyzed" included those who underwent surgery.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Between Days 7 and 21 of the 3rd cycle of neoadjuvant treatment, thereafter, every 9 weeks during adjuvant treatment and then after adjuvant treatment every 3 months until Month 25

| End point values | Capecitabine+ Oxaliplatin+Tra- stuzumab | | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 31 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 90.32 (74.25 to 97.96) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Pathological Complete Response (pCR)

| | |
|-----------------|--|
| End point title | Percentage of Participants With Pathological Complete Response (pCR) |
|-----------------|--|

End point description:

pCR was defined as an absence of any invasive cancer cell of the primary tumor after the time of major neoadjuvant chemotherapy, with or without surgery. ITT population.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Between Days 7 and 21 of the 3rd cycle of neoadjuvant treatment, thereafter, every 9 weeks during adjuvant treatment and then after adjuvant treatment every 3 months until Month 25

| End point values | Capecitabine+ Oxaliplatin+Tra- stuzumab | | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 36 | | | |
| Units: percentage of participants | | | | |
| number (confidence interval 95%) | 8.33 (1.75 to 22.47) | | | |

Statistical analyses

No statistical analyses for this end point

Secondary: Percentage of Participants With Objective Response

| | |
|-----------------|--|
| End point title | Percentage of Participants With Objective Response |
|-----------------|--|

End point description:

An objective response was defined as either a complete response (CR) or a partial response (PR). Using the Response Evaluation Criteria in Solid Tumors (RECIST), CR was defined as the disappearance of all target lesions and all non-target lesions, normalization of tumor marker level, and no new lesions. PR was defined as the disappearance of all target lesions and persistence of greater than or equal to (\geq) 1 non-target lesions and/or the maintenance of tumor marker level above the normal limits, or, at least a 30% decrease in the sum of the longest diameter of target lesions, and no new lesions or unequivocal progression of existing non-target lesions. ITT population.

| | |
|----------------|-----------|
| End point type | Secondary |
|----------------|-----------|

End point timeframe:

Between Days 7 and 21 of the 3rd cycle of neoadjuvant treatment, thereafter, every 9 weeks during adjuvant treatment and then after adjuvant treatment every 3 months until Month 25

| End point values | Capecitabine+ Oxaliplatin+Tra- stuzumab | | | |
|-----------------------------------|---|--|--|--|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 36 | | | |
| Units: percentage of participants | | | | |
| number (not applicable) | 38.89 | | | |

Statistical analyses

No statistical analyses for this end point

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Before Day 1 of each cycle until Month 25

Adverse event reporting additional description:

The safety analysis included all participants in the ITT population who received at least 1 dose of the study drugs.

| | |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

Dictionary used

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|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

| | |
|--------------------|------|
| Dictionary version | 17.1 |
|--------------------|------|

Reporting groups

| | |
|-----------------------|--------------------------------------|
| Reporting group title | Capecitabine+Oxaliplatin+Trastuzumab |
|-----------------------|--------------------------------------|

Reporting group description:

Participants received 3 cycles of capecitabine (1,000 mg/m² tablet p.o twice daily, Days 1-14)/oxaliplatin (130 mg/m² as a 120-minute IV infusion Day 1 of the cycle)/trastuzumab (8 mg/kg on Day 1, followed by doses of 6 mg/kg as IV infusion) (XELOX-trastuzumab) as neoadjuvant treatment, every 3 weeks, thereafter, they were assessed for surgery. After surgery, participants received 3 cycles of XELOX-trastuzumab as treatment adjuvant to the surgery, thereafter, another 12 cycles of trastuzumab as monotherapy, was administered every 3 weeks, until disease progression or death.

| Serious adverse events | Capecitabine+Oxaliplatin+Trastuzumab | | |
|---|--------------------------------------|--|--|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 22 / 36 (61.11%) | | |
| number of deaths (all causes) | 8 | | |
| number of deaths resulting from adverse events | | | |
| Injury, poisoning and procedural complications | | | |
| Procedural complication | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Anastomotic leak | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vascular disorders | | | |
| Peripheral ischaemia | | | |

| | | | |
|--|----------------|--|--|
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Hypovolaemic shock | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Cardiac disorders | | | |
| Cardiogenic shock | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Nervous system disorders | | | |
| Encephalopathy | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| General disorders and administration site conditions | | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 1 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Multi-organ failure | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Pyrexia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Sudden death | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

| | | | |
|---|-----------------|--|--|
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences causally related to treatment / all | 6 / 6 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal obstruction | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Intestinal ischaemia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Dysphagia | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Vomiting | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Oesophageal perforation | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Localised intra-abdominal fluid collection | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Pneumothorax | | | |

| | | | |
|---|----------------|--|--|
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pleural effusion | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Psychiatric disorders | | | |
| Schizoaffective disorder | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Renal and urinary disorders | | | |
| Renal failure acute | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Infections and infestations | | | |
| Sepsis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Postoperative wound infection | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Appendicitis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 0 | | |
| Pneumonia | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences causally related to treatment / all | 0 / 2 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

| | | | |
|---|----------------|--|--|
| Abdominal sepsis | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |
| Septic shock | | | |
| subjects affected / exposed | 1 / 36 (2.78%) | | |
| occurrences causally related to treatment / all | 0 / 1 | | |
| deaths causally related to treatment / all | 0 / 1 | | |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events | Capecitabine+Oxalip latin+Trastuzumab | | |
|---|--|--|--|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 35 / 36 (97.22%) | | |
| Investigations | | | |
| Alanine aminotransferase increased | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 5 | | |
| Ejection fraction decreased | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Aspartate aminotransferase increased | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 4 | | |
| Vascular disorders | | | |
| Hypertension | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Nervous system disorders | | | |
| Neurotoxicity | | | |
| subjects affected / exposed | 10 / 36 (27.78%) | | |
| occurrences (all) | 16 | | |
| Paraesthesia | | | |
| subjects affected / exposed | 6 / 36 (16.67%) | | |
| occurrences (all) | 11 | | |
| Dysaesthesia | | | |

| | | | |
|--|------------------|--|--|
| subjects affected / exposed | 7 / 36 (19.44%) | | |
| occurrences (all) | 18 | | |
| Neuropathy peripheral | | | |
| subjects affected / exposed | 6 / 36 (16.67%) | | |
| occurrences (all) | 9 | | |
| Dysgeusia | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 5 | | |
| Peripheral sensory neuropathy | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 6 | | |
| Blood and lymphatic system disorders | | | |
| Anaemia | | | |
| subjects affected / exposed | 11 / 36 (30.56%) | | |
| occurrences (all) | 13 | | |
| Thrombocytopenia | | | |
| subjects affected / exposed | 4 / 36 (11.11%) | | |
| occurrences (all) | 16 | | |
| Neutropenia | | | |
| subjects affected / exposed | 7 / 36 (19.44%) | | |
| occurrences (all) | 16 | | |
| General disorders and administration site conditions | | | |
| Asthenia | | | |
| subjects affected / exposed | 24 / 36 (66.67%) | | |
| occurrences (all) | 61 | | |
| Pyrexia | | | |
| subjects affected / exposed | 10 / 36 (27.78%) | | |
| occurrences (all) | 13 | | |
| Mucosal inflammation | | | |
| subjects affected / exposed | 8 / 36 (22.22%) | | |
| occurrences (all) | 9 | | |
| Gastrointestinal disorders | | | |
| Diarrhoea | | | |
| subjects affected / exposed | 29 / 36 (80.56%) | | |
| occurrences (all) | 68 | | |
| Constipation | | | |

| | | | |
|---|------------------|--|--|
| subjects affected / exposed | 6 / 36 (16.67%) | | |
| occurrences (all) | 6 | | |
| Abdominal pain upper | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 8 | | |
| Gastrooesophageal reflux disease | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 2 | | |
| Abdominal pain | | | |
| subjects affected / exposed | 9 / 36 (25.00%) | | |
| occurrences (all) | 12 | | |
| Nausea | | | |
| subjects affected / exposed | 17 / 36 (47.22%) | | |
| occurrences (all) | 29 | | |
| Dyspepsia | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Dysphagia | | | |
| subjects affected / exposed | 5 / 36 (13.89%) | | |
| occurrences (all) | 13 | | |
| Vomiting | | | |
| subjects affected / exposed | 15 / 36 (41.67%) | | |
| occurrences (all) | 26 | | |
| Hepatobiliary disorders | | | |
| Hyperbilirubinaemia | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 3 | | |
| Respiratory, thoracic and mediastinal disorders | | | |
| Epistaxis | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 13 | | |
| Dyspnoea | | | |
| subjects affected / exposed | 3 / 36 (8.33%) | | |
| occurrences (all) | 4 | | |
| Catarrh | | | |

| | | | |
|--|---------------------|--|--|
| subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 7 | | |
| Rhinorrhoea subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 3 | | |
| Skin and subcutaneous tissue disorders | | | |
| Erythema subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Pruritus subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Nail disorder subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 4 | | |
| Rash subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Palmar-plantar erythrodysaesthesia syndrome subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 4 | | |
| Psychiatric disorders | | | |
| Anxiety subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Musculoskeletal and connective tissue disorders | | | |
| Arthralgia subjects affected / exposed occurrences (all) | 3 / 36 (8.33%) 5 | | |
| Pain in extremity subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Muscle spasms subjects affected / exposed occurrences (all) | 2 / 36 (5.56%) 2 | | |
| Metabolism and nutrition disorders | | | |

| | | | |
|-----------------------------|------------------|--|--|
| Hypokalaemia | | | |
| subjects affected / exposed | 2 / 36 (5.56%) | | |
| occurrences (all) | 4 | | |
| Decreased appetite | | | |
| subjects affected / exposed | 15 / 36 (41.67%) | | |
| occurrences (all) | 30 | | |

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported